U.S. PATENTS

U.S. PATENT NUMBER	INVENTOR(S)
4,009,282	Voorhees
4,016,036	Green, et al.
4,088,756	Voorhees
4,201,788	Voorhees, et al.
4,207,315	Voorhees, et al.
4,304,866	Green, et al.
4,485,096	Bell
4,604,346,	Bell, et al.
4,673,649	Boyce, et al.
4,940,666	Boyce, et al.
5,232,848	Wolfe, et al.
5,292,655	Wille, Jr.
5,326,699	Torishima, et al.
5,328,844	Moore
5,686,307	Wille, Jr.
5,834,312	Wille, Jr.
5,871,909	ANG.strom, et al.
6,063,606	Petkovich, et al.

FOREIGN PATENT DOCUMENTS

Country	Patent No.	Inventor(s)
	NONE	

OTHER DOCUMENTS

1. "Production of Epidermal Sheets in a Serum Free Culture System: A further appraisal of the role of extracellular calcium," *Journal of Dermatological Science*, 3, Boisseau, et al., Elseiver Science Publishers V.V. (1992) 111-120.

2. "Reagents, Suppliers and Media Formulations," *Catalogue of Cell Lines & Hybridomas*, American Type Culture Collection, 6th Ed. 1988, pp. 342-343.

3. "Production and auto-induction of transforming growth factor-α in human keratinocytes," Coffey, Jr., et al., *Nature*, vol. 328, 27 August 1987, pp. 817-820.

4. "Growth and Differentiation of Human Keratinocytes Without a Feeder Layer or Conditioned Medium," Peehl, et al., *In Vitro*, 1616: 516-525; 1980.

5. "Improved Medium and Culture Conditions for Clonal Growth with Minimal Serum Protein and for Enhanced Serum-Free Survival of Swiss 3T3 Cells," Shipley, et al., *In Vitro*, vol. 17, No. 8,. August 1981: 1981 Tissue Culture Association, Inc., pp. 656-670.

6. "Buffer Combinations for Mammalian Cell Culture," *Science*, Vol. 174, pp. 500-503.

7. "Cultured Cells for Treatment of Disease," Green, *Scientific American*, Nov. 1991, pp. 96-102.

8. "Culture of Human Keratinocytes in Defined Serum-Free Medium," Judd, et al., *Focus,* 19 No. 1 (1997), pp. 2-5.

9. "Cultured Composite Skin Grafts: Biological Skin Equivalents Permitting Massive Expansion," Nanchahal, et al., *The Lancet*, July 22, 1989, pp. 191-193.

10. "Growth of Cells in Defined Environments: The Roleof Endogenous Production of Insulin-like Growth Factors," Nissley, et al., *Growth & Differentiation of Cells in a Defined Environment* (1985) pp. 337-344.

11. "Long-term restoration of damaged corneal surfaces with autologous cultivated corneal epithelium," Pellegrini, et al., *The Lancet*, vol. 349, April 5, 1997, pp. 990-993.

12. "Calcium-Regulated Differentiation of Normal Human Epidermal Keratinocytes in Chemically Defined Clonal Culture and Serum-Free Serial Culture," Boyce, et al., *The Journal of Investigative Dermatology*, Boyce, et al., vol. 81, no. 1 Supplement (1983), pp. 33s-40s.

13. "Cultivating a Cure for Blindness," Hodson, *Nature*, vol. 387, May 1997, p. 449.

14. "Clonal Growth of Normal Human Epidermal Keratinocytes in a Defined Medium," Tsao, et al., *Journal of Cellular Physiology* 110:219-229 (1982).

15. "Ability of Normal Human Keratinocytes that Grow in a Culture in Serum-Free Medium to be Derived from Suprabasal Cells," Wilke, et al., *Journal of the National Cancer Institute*, vol. 80, no. 16, Oct. 1988, pp. 1299-1304.

16. "Biologic Mechanisms for the Regulation of Normal Human Keratinocyte Proliferation and Differentiation," Wilke, et al., *American Journal of Pathology*, vol. 131, April 1988, pp. 171-181.

17. "Effects of Growth Factors, Hormones, Bacterial Lipopolysaccharides, and Lipotechoic Acids on the Clonal Growth of Normal Ureteral Epithelial Cells in Serum-Free Culture," Wille, et al., *Journal of Cellular Physiology*, 150:52-58 (1992).

18. "Integrated Control of Growth and Differentiation of Normal Human Prokeratinocytes Cultured in Serum-Free Medium: Clonal Analyses, Growth Kinetics, and Cell Cycle Studies," Wille, Jr., et al., *Journal of Cellular Physiology*, 121:31-44 (1984).

19. "Propagation of Differentiating Normal Human Tracheobronchial Epithelial Cells in Serum-Free Medium," Chopra, et al., *Journal of Cellular Physiology* 130: 173-181 (1987).

20. "Reversible Inhibition of Normal Human Prokeratinocyte Proliferation of Type β Transofrming Growth Factor-Growth Inhibitor in Serum-free Medium," Shipley, et al., *Cancer Research* 46, 2068-2071, April, 1986.

21. "Serum-Free Cultures of Normal Human Gingival Keratinocytes (HGK),", Wille, et al., *Journal of Dental Research*, 68, 1019, #1216.

22. "Two Functionally Distinct Classes of Growth Arrest States in Human Prokeratinocytes that Regulate Clonogenic Potential," Pittelkow, et al., *Journal of Investigative Dermatology*, vol. 4, April, 1986, pp. 410-417.

23. Moses, et al. "Growth & Differentiation of Cells in Defined Enviroment (1985) pp. 373-378.

24. Booyens, et al, "Prostaglandins Leukot. Md.," Jul. 1984, 15 (1) pp. 15-33 (Biosis Abstract #84298492).

25. The Merck Index, 10th edition, 1983, p. 1172.

26. Boyce & Ham, *J. Invest. Dermatol.* 81:33-40, 1983 Ca-Reg. differentiation of normal human epid. Keratin In chemical & serum defined Med.

27. "All-Trans Retinoic Acid Stimulates Growth of Adult Human Keratinocytes Cultured in Growth Factor-Deficient Medium, Inhibits Production of Thrombosondin in Fibronectin, and Reduces Adhesion," Varani, et al. *The Society for Investigative Dermatology, Inc.*, 0022-202X/89/S03.50 (1989)

28. Rikimaru, et al. "Growth of malignant and nonmalignant human squamous cells in a protein-free defined medium, *In Vitro Cell Dev. Biol.*, 26(9):849-56, Sept. 1990 (Medline Abstract)

29. Diaz, et al. "Regulation of vascular endothelial growth factor expression in human keratinocytes by retinoids, *J. Biol. Chem.* 275(1):642-50, Jan. 7, 2000 (Medline Abstract)

30. Stoll, et al. "Retinoid regulation of heparin-binding EGF-like growth factor gene expression in human keratinocytes and skin," *Exp. Dermatol.* 7(6):3917, Dec. 1998 (Medline Abstract)

31. Marcello, et al., "Retinoic acid stimulates essential fatty acid-supplemented human keratinocytes in culture," *J. Invest. Dermatol.*, 108(5):758-62 May 1997 (Medline Abstract)

32. Jetten "Multi-stage program of differentiation in human epidermal keratinocytes: regulation by retinoids," *J. Invest. Dermatol.*, 85(5):44S-46S Nov. 1990 (Medline Abstract)

33. Jee, et al., "Growth and characterization of normal human keratinocytes in F12 serum-free medium," *J. Formos Med. Assoc.* 89(7):559-64 July 1990 (Medline Abstract)

34. Varani, "Preservation of human skin structure and function in organ culture," *Histol. Histopathol.* 13(3):775-83 July 1998 (Medline Abstract)

35. Siegenthaler, et al. "Retinol and retinal metabolism. Relationship to the state of differentiation of cultured human keratinocytes," *Biochem J.* 268(2):371-8 June 1, 1990 (Medline Abstract)

36. Lachgar, et al. "Inhibitory effects of retinoids on vascular endothelial growth factor production by cultured human skin keratinocytes," *Dermatology* 199 Suppl. 1:25-7 1999 (Medline Abstract)

37. Imanishi, et al. "Growth factors: importance in wound healing and maintenance of transparency of the cornea," *Prog. Retin Eye Res.* 19(1):113-29 Jan. 2000 (Medline Abstract)

38. Johnson, et al. "Persistence of fetal bovine serum proteins in human keratinocytes," *J. Burn Care Rehabil.*, 11(6) 504-9 Nov.-Dec. 1990 (Medline Abstract)

39. Schwartz "In vitro growth changes of oral human keratinocytes after treatment with carotenoids, retinoid, and/or DMBA," *Nutr. Cancer*, 33(1):58-68 1999 (Medline Abstract)

40. Sass, et al. "Metabolism of topical retinaldehyde and retinol by mouse skin in vivo: predominant formation of retinyl esters and identification of 14-hydroxy-4, 4-retro-retinol," *Exp. Dermatol.* 5(5):267-71, Oct. 1996 (Medline Abstract)

41. Marikar, et al. "Retinoic acid receptors regulate expression of retinoic acid 4-hydroxylase that specifically inactivates all-trans retinoic acid in human keratinocyte HaCaT cells," *J. Invest. Dermatol.*, 111(3):434-9 Sept. 1998 (Medline Abstract)

42. Griffiths, et al. "Short-term retinoic acid treatment increases in vivo, but decreases in vitro, epidermal transglutaminase-K enzyme activity and immunoreactivity," *J. Invest Dermatol.* 99(3):283-8 Sept. 1992 (Medline Abstract)

43. Duell, et al. "Human skin levels of retinoic acid and cytochrome P-450-derived 4-hydroxyretinoic acid after topical application of retinoic acid in vivo compared to concentrations required to stimulate retinoic acid receptor-mediated transcription in vitro," *J. Clin. Invest.* 90(4): 1269-74 Oct. 1992 (Medline Abstract)

44. Duell, et al. "Unoccluded retinol penetrates human skin in vivo more effectively than unoccluded retinyl palmitate or retinoic acid," *J. Invest. Dermatol.* 109(3):301-5 Sept. 1997 (Medline Abstract)

45. Kang, et al. "Liarozole inhibits human epidermal retinoic acid 4-hydroxylase activity and differentially augments human skin responses to retinoic acid and retinol in vivo," *J. Invest. Dermatol.* 107(2):183-7 Aug. 1996 (Medline Abstract)

46. Kurlandsky, et a; "Auto-regulation of retinoic acid biosynthesis through regulation of retinol esterification in human keratinocytes," *J. Biol. Chem.* 271 (26):15346-52 June 28, 1996 (Medline Abstract)

47. Varani, et al. "A direct comparison of pharmacologic effects of retinoids on skin cells in vitro and in vivo," *Skin Pharmacol.* 4(4):254-61 1991 (Medline Abstract)

48. Varani, et al. "Retinoic acid stimulation of human dermal fibroblast proliferation is dependent on suboptimal extracellular Ca2+ concentration," *Am. J. Pathol.* 136(6):1275-81 June 1990 (Medline Abstract)

49. Varani, et al. "All-trans retinoic acid stimulates growth and extracellular matrix production in growth-inhibited cultured human skin fibroblasts," *J. Invest. Dermatol.* 94(5):717-23 May 1990 (Medline Abstract)

50. Wang, et al. "Ultraviolet irradiation of human skin causes functional vitamin A deficiency, preventable by all-trans retinoic acid pre-treatment," *Nat. Med.* 5(4):418-22 April 1999 (Medline Abstract)

51. Xiao, et al. "Identification of heparin-binding EGF-like growth factor as a target in intercellular regulation of epidermal basal cell growth by suprabasal retinoic acid receptors," *EMBO J.* 18(6):1539-48 March 15, 1999 (Medline Abstract)

52. Griffiths, et al. "Mechanisms of action of retinoic acid in skin repair," *Br. J. Dermatol.* 127 Suppl 4:21-4 Sept. 1992 (Medline Abstract)

53. Varani, et al. "Induction of proliferation of growth-inhibited keratinocytes and fibroblasts in monolayer culture by sodium lauryl sulfate: comparison with all-trans retinoic acid," *J. Invest. Dermatol.* 97(5):917-21 Nov. 1991 (Medline Abstract)

54. Fligiel, et al. "Modulaton of growth in normal and malignant melanocytic cells by all-trans retinoic acid," *J, Cutan Pathol.* 19(1):27-33 Feb. 1992 (Medline Abstract)

55. Varani, et al. "Inhibition of epithelial cell adhesion by retinoic acid. Relationship to reduced extracellular matrix production and alterations in Ca2+ levels," *Am. J. Pathol.* 138(4):887-95 April 1991 (Medline Abstract)

56. Varani, et al. "Modulation of Ca2+ levels in keratinocytes by all-trans retinoic acid," *Pathobiology* 60(2):93-9 1992 (Medline Abstract)

57. Varani, et al. "Molecular mechanisms of intrinsic skin aging and retinoid-induced repair and reversal," *J. Invest. Dermatol. Symp. Proc.* 3(1):57-60 Aug. 1998 (Medline Abstract)

58. Tavakkol, et al. "Expression of growth hormone receptor, insulin-like growth factor 1 (IFG-1) and IFG-1 receptor mRNA and proteins in human skin," *J. Invest. Dermatol.* 99(3):343-9 Sept. 1992 (Medline Abstract)

59. Fisher, et al. "Molecular mechanisms of retinoid actions in skin," *FASEB J.* 10(9):1002-13 July 1996 (Medline Abstract)

60. Sasaki, et al. "Enhancement by 1 alpha,25-dihydrocyvitamin D3 of chemically induced transformation of BALB 3T3 cells without induction of ornithine decarboxylase or activation of protein kinase C1," *Cancer Res.* 46(2):604-10 Feb. 1986 (Medline Abstract)

61. Kamata, et al. "Growth of normal oral keratinocyates and squamous cell carcinoma cells in a novel protein-free defined medium," *In Vitro Cell Dev. Biol Anim.* 35(10):63-41 Nov.-Dec. 1999 (Medline Abstract)

62. Goi, et al "DNA damage-associated dysregulation of the cell cycle and apoptosis control in cells with germ-line p53 mutation," *Cancer Res.* 57(10):1895-902 May 15, 1997 (Medline Abstract)

63. Kurata, et al. "Effect of eicosapentaenoic acid and arachidonic acid on mouse peritoneal exudate cells and its characteristics," *Yakugaku Zassi* 106(11):1040-4 Nov. 1986 (Japanese language—copy not available) (Medline report)

64. Kamata, et al. "Growth-inhibitory effects of epidermal growth factor and overexpression of its receptors on human squamous cell carcinomas in culture," *Cancer Res.* 46(4 Pt 1):1648-53 April 1986 (Medline Abstract)

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